November 1963

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Technical Report No. 32

University of Minnesota

Minneapolis, Minnesota

* This research was supported in part under Grant Number 2G-43(C7+8) of the National Institutes of Health, under Grant Number MYP-5106 of the National Institute of Mental Health, U. S. Public Health Service and under Grant Number Nonr 710(31) of the Office of Naval Research.

AN APPLICATION OF MULTIVARIATE ANALYSIS TO SOME TRANQUILIZER COMPARISON EXPERIMENTS

by

Constance van Eeden,[1] Gordon T. Heistad[2] and Charles H. Kraft[3]

1. Introduction

Two groups of patients were rated by the Wittenborn psychiatric rating scale before and after treatment. Group I, 16 patients, were administered the tranquilizer thioridazine (Mellaril), Group II, 17 patients, were administered the tranquilizer carphenazine (Proketazine). The Wittenborn psychiatric rating scale is an instrument which was designed to detect the severity of symptoms in each of nine areas, which we will call sub-scales; they are in fact symptom clusters derived on the basis of a factor analysis done by Wittenborn on a rather different population than that used in this study [3].

To test whether there is any difference between the two treatments, the changes in the Wittenborn sub-scales (pre-treatment minus post-treatment) were computed. It was assumed that these changes were, for the patients in each group, independent observations from multivariate normal populations. It was further assumed that the changes in one group were independent of those in the other group and that the population covariance matrices were the same for the two groups. Under these assumptions a difference between the treatments would appear

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as a difference between the means.

The appropriate test that this difference is zero is Hotelling's T^2 [1, pp. 108-109]. This test is the analogue of Student's t for the univariate case and is a distance between the group (vector) means. The mean for each group defines a point in 9-dimensional space, each dimension being a sub-scale of the Wittenborn. If the distance between these points is large, in units defined by the estimated covariance matrix, Hotelling's T^2 will be large and the test will reject the hypothesis of no treatment difference.

It is important to note that this distance can be large in many ways. For instance one drug might produce relative changes in the sub-scales of the Wittenborn which are the same as those for the second drug but greater in magnitude. That is the vectors of means would have the same direction but different lengths. On the other hand it could be that the magnitude of change is about the same for the two drugs but that one drug produces changes on a different set of sub-scales than does the other drug. That is the two vectors of means have different directions.

In the first case it could be said that one drug is more effective than the other, but they each affect the same symptoms. In the second case the drugs could be said to be equally effective (over-all) but that they affect different symptoms. Of course the difference might not clearly be one or the other of these.

2. Results

The data are given on page 10 for drug I and on page 11 for drug II. The observed means and covariance matrices for each of the two groups are given on page 12. These means are graphed in Figure 1 and the observed mean difference between the two groups (Group I minus Group II) is tabled, with the combined covariance matrix, in Table 1.

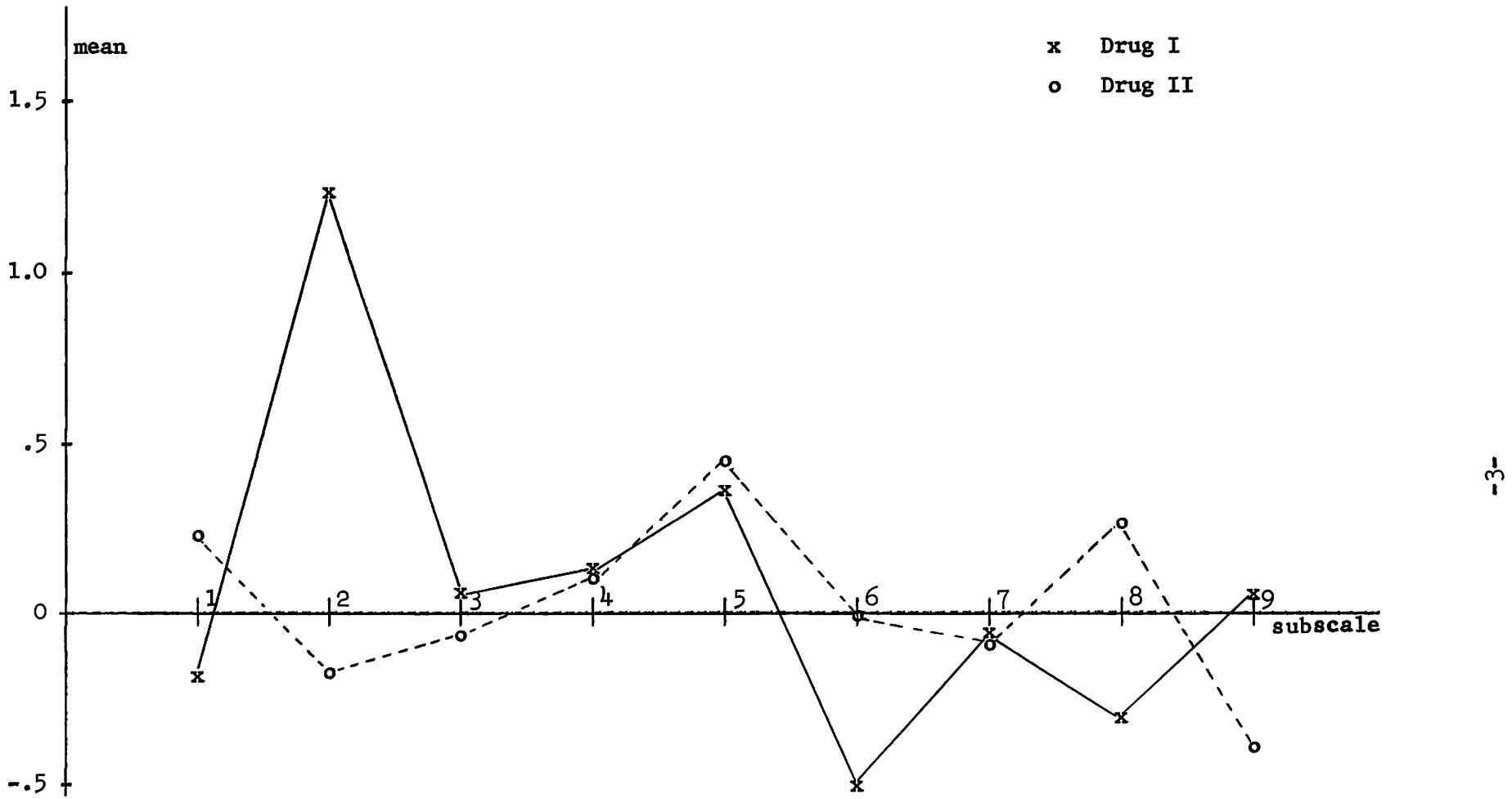

Figure 1: Observed means for Drug I and Drug II.

For this data the null hypothesis: there is no difference between the drugs, is accepted. The observed level of significance is .6.

Table 1: Combined covariance matrix and difference between the means for the two drugs.

difference between means (D_I-D_{II})	covariance matrix									
	subscale ↓ →	1	2	3	4	5	6	7	8	9
-.43	1	1.85	.66	.30	1.67	.75	.69	1.45	.87	1.09
1.43	2		7.34	-.98	4.12	-.20	.26	-1.58	.36	.73
.12	3			2.90	-.90	.33	.69	.77	-.11	.79
.01	4				10.24	-.54	.39	-.44	2.16	4.38
-.09	5					3.35	.39	1.74	.34	-.20
-.50	6						1.35	.50	.89	1.21
.00	7							2.77	.58	.67
-.60	8								1.90	1.59
.47	9									5.39

3. Confidence intervals

Scheffé's simultaneous confidence intervals for the difference between the means were computed. Because H_o was accepted the intervals all contain the origin. They are included to give an idea of the precision of the experiment.

For a description and proof of this method see Scheffé [2, pp. 68-70]. He there shows that the set of all points, in 9-dimensional space, that would be accepted as null-hypothesis for the difference between the changes produced by the two drugs, is an ellipsoid. He further shows that a confidence interval for any linear combination of the components of the difference between the group means can be obtained by projecting the ellipsoid onto a line defined by the particular linear combination. Given in Figure 2 are these projections on the

axes corresponding to each subscale of the Wittenborn. These confidence intervals are for $\alpha = .05$. The half-lengths of these intervals are in the center column of Table 2. For comparison there are also, in Table 2, given the corresponding half-lengths for levels of significance $\alpha = .01$ and $\alpha = .10$.

Table 2: Half-lengths of simultaneous confidence intervals for the difference between the drugs.

subscale \ α	.01	.05	.10
1	3.0	2.5	2.3
2	6.0	5.0	4.6
3	3.7	3.1	2.8
4	7.1	5.9	5.4
5	4.0	3.4	3.1
6	2.6	2.2	2.0
7	3.7	3.1	2.8
8	3.0	2.5	2.3
9	5.1	4.3	3.9

If the sample sizes had been doubled (to 32 and 34) the corresponding half-lengths would be approximately .6 times those in Table 2 for all three levels of significance. Had the sample sizes been quadrupled the half-lengths would be about .4 times those given. The comparisons assume that changes in the sample sizes would not produce large changes in the covariance matrices.

4. Power of the test

The power of Hotelling's T^2-test is given by the non-central F-distribution ([1, p. 114] and [2, p. 418]). The non-centrality parameter is given by

$$\delta = \sqrt{\frac{N_1 N_2}{N_1+N_2} \Delta' \Sigma^{-1} \Delta} \quad ,$$

where N_1 and N_2 are the sample sizes, Σ is the population covariance matrix

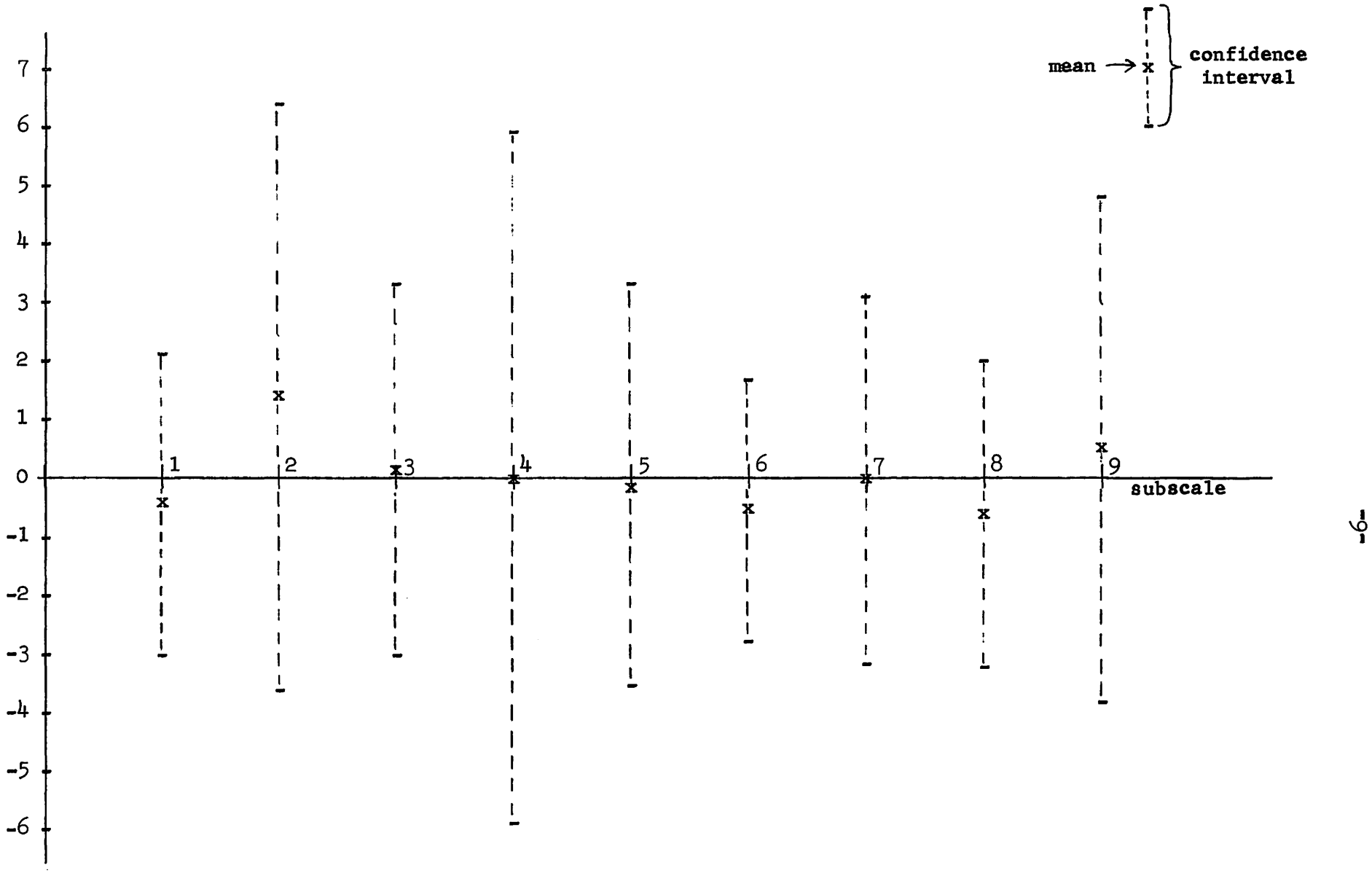

Figure 2: Simultaneous confidence intervals and means for the difference between the drugs.

$(D_I - D_{II})$ $(\alpha = .05)$

and Δ is the difference between the population means; this difference Δ is a vector of 9 variables (the nine differences between the changes on the nine Wittenborn subscales).

The graph in Figure 3 gives the power as a function of c, where Δ is taken to be c times the vector of standard deviations. If the true difference between the two treatments is half of a standard deviation on each subscale the power is .38 if each sample size is 15; the power is .55 if each sample size is 20; and the power is .87 if each sample size is 35. These calculations were made assuming that the covariance matrix observed here is the (common) population covariance matrix; the level of significance is .05. The corresponding curves for $\alpha = .01$ are given in Figure 4.

5. Remark

The null hypothesis for Hotelling's T^2 is that of no difference between the mean vectors. It is of interest to have a test which would be insensitive to a difference only in magnitude of change and sensitive to difference in direction of change. Such a test would be more appropriate to the question: "Is the set of symptoms on which drug I acts different from those on which drug II acts?". The likelihood ratio test for H_o: $\mu_I = a\mu_{II}+b$ has been derived and will be the subject of a separate report.

The authors wish to thank Richard Borden for the care with which he carried out the computations for this report.

6. References

[1] Anderson, T. W., An introduction to multivariate statistical analysis, J. Wiley and Sons, Inc., New York, 1958.

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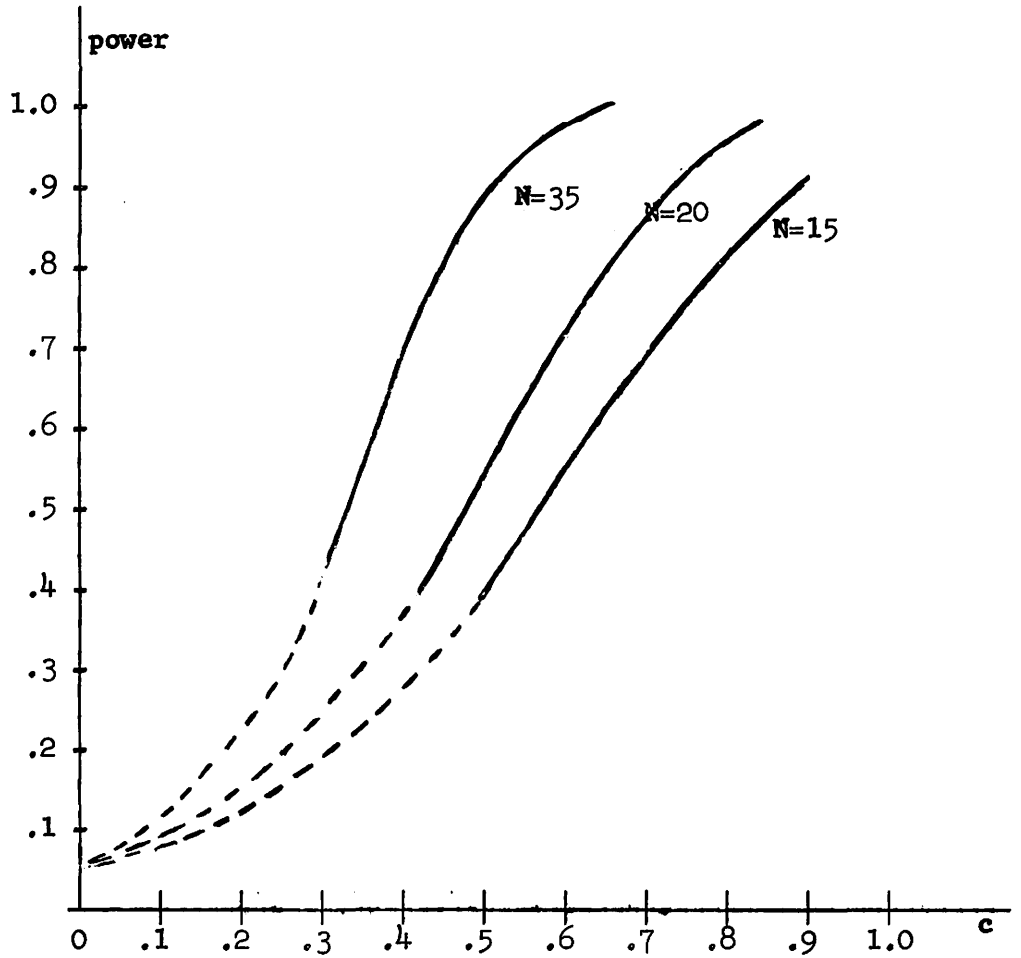

Figure 3: Power of Hotelling's T^2 for sample sizes $N_1 = N_2 = 15$; 20 and 35 as a function of c, where $\Delta = c(\sigma_1,\ldots,\sigma_9)$ ($\alpha = .05$)

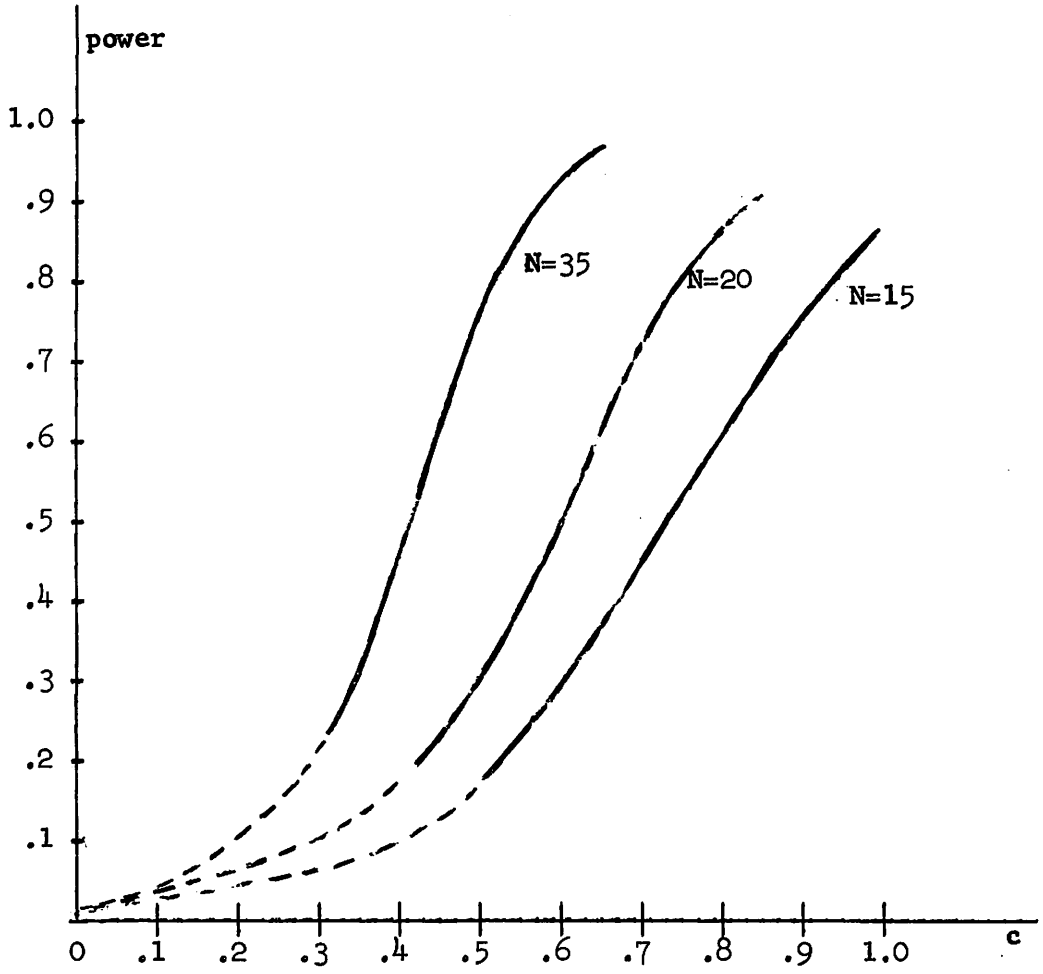

Figure 4: Power of Hotelling's T^2 for sample sizes $N_1 = N_2 = 15$; 20 and 35 as a function of c, where $\Delta = c(\sigma_1,\ldots,\sigma_9)$ ($\alpha = .01$)

Data Drug I thioridazine (Mellaril)

Patient	Pretreatment subscale									Posttreatment subscale								
	1	2	3	4	5	6	7	8	9	1	2	3	4	5	6	7	8	9
I.1	1	6	1	1	3	1	1	1	1	2	9	1	4	6	1	1	1	1
I.2	1	7	1	3	3	1	1	2	1	1	8	1	2	2	1	1	1	1
I.3	1	5	1	2	4	2	1	2	3	2	5	1	1	1	1	1	1	1
I.4	1	6	2	4	4	3	1	4	1	3	2	1	2	3	3	3	5	2
I.5	2	5	4	2	1	1	2	1	2	2	4	1	4	1	2	1	3	4
I.6	2	4	3	5	3	5	5	5	4	2	4	3	5	3	5	5	5	4
I.7	1	5	1	2	2	1	1	1	1	1	4	1	3	1	1	1	2	1
I.8	2	9	1	6	2	2	2	3	2	1	4	1	5	1	2	1	4	2
I.9	1	6	3	8	3	2	1	3	9	1	6	1	4	4	2	1	3	2
I.10	2	7	1	8	2	2	1	3	2	2	2	5	3	1	5	3	4	3
I.11	3	7	1	9	4	2	4	4	9	3	4	1	6	7	3	5	4	5
I.12	1	1	1	2	2	1	3	1	1	2	4	1	5	3	5	3	4	6
I.13	4	9	1	6	8	1	5	3	2	3	9	1	8	3	1	1	2	1
I.14	1	6	1	2	2	1	1	1	1	1	3	2	1	1	1	1	1	1
I.15	2	4	1	4	2	4	3	5	1	1	3	1	9	1	3	3	5	5
I.16	2	5	1	9	1	6	3	9	9	3	1	1	9	2	7	5	8	9

Data Drug II carphenazine (Proketazine)

Patient	Pretreatment subscale									Posttreatment subscale								
	1	2	3	4	5	6	7	8	9	1	2	3	4	5	6	7	8	9
II.1	1	1	1	3	3	1	1	1	2	2	6	1	2	1	2	1	1	4
II.2	1	6	1	3	2	2	1	3	1	3	3	1	5	3	4	3	4	5
II.3	1	3	1	2	3	1	1	2	1	1	3	1	1	1	1	1	1	1
II.4	3	9	1	5	5	2	5	2	2	2	9	1	7	3	2	2	4	3
II.5	2	6	4	2	2	1	1	1	1	2	9	1	2	2	1	1	2	1
II.6	2	6	1	4	5	1	4	4	3	1	9	1	6	2	1	1	2	2
II.7	1	5	1	3	2	1	1	1	1	1	9	1	6	2	1	1	2	1
II.8	3	9	4	9	1	3	2	6	3	3	9	1	8	2	2	3	6	1
II.9	3	5	1	8	1	4	4	7	4	2	4	1	3	3	2	4	3	3
II.10	2	9	1	8	3	1	1	3	2	3	7	7	4	6	2	4	3	2
II.11	2	5	1	2	2	2	3	3	1	4	9	3	9	2	3	3	4	5
II.12	4	9	1	7	6	1	7	3	1	3	6	1	4	3	1	7	2	1
II.13	1	4	1	1	1	1	1	1	1	3	5	1	3	1	2	3	1	2
II.14	3	9	1	9	2	2	2	4	3	1	5	1	4	1	2	1	3	1
II.15	2	9	4	4	3	2	1	3	1	1	9	3	8	2	1	1	3	1
II.16	6	9	1	9	3	2	4	5	2	1	9	1	3	2	1	1	2	1
II.17	2	6	1	4	1	3	1	3	1	2	2	1	6	1	2	4	4	3

Means and Covariances Matrices

Drug I

means	covariance matrix: subscale ↓ →	1	2	3	4	5	6	7	8	9
-.19	1	.70	.25	-.12	-.31	.54	.23	.72	.14	.15
1.25	2		6.47	-1.15	3.77	.63	.00	-1.45	.08	.72
.06	3			2.06	-1.14	-.43	.63	.60	-.18	.73
.13	4				7.32	-.32	-.47	-1.73	.44	4.79
.38	5					3.98	.80	1.49	.59	-.63
-.50	6						1.73	.50	.97	1.30
-.06	7							2.06	.18	.14
-.31	8								1.30	1.62
.06	9									7.80

Drug II

means	covariance matrix: subscale ↓ →	1	2	3	4	5	6	7	8	9
.24	1	2.94	1.04	.70	3.53	.94	1.13	2.14	1.55	1.98
-.18	2		8.15	-.82	4.46	-.97	.50	-1.70	.62	.74
-.06	3			3.68	-.68	1.03	.75	.93	-.04	.85
.12	4				12.99	-.75	1.19	.76	3.78	3.99
.47	5					2.76	.00	1.97	.10	.21
.00	6						1.00	.50	.81	1.13
-.06	7							3.43	.96	1.16
.29	8								2.47	1.57
-.41	9									3.13